UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,956	09/18/2003	Maria Alexandra Glucksmann	MPI00-368P1RCN1M	8337

7590 10/17/2005

MILLENNIUM PHARMACEUTICALS, INC.
Intellectual Property Department
75 Sidney Street
Cambridge, MA 02139

EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 10/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/665,956	GLUCKSMANN ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23,47-52 and 72* is/are pending in the application.

4a) Of the above claim(s) *8-11,13-23,47-52 and 72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/06/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

300

1) Claims 1 to 23, 47 to 52 and 72 are pending in the instant application.

2) Claims 8 to 11, 13 to 23, 47 to 52 and 72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made in the correspondence filed 06 September of 2005. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3) The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on each of pages 9 to 11, 22 and 23 therein, for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01(p), which states that:

> "When a patent application with embedded hyperlinks and/or other forms of browser-executable code issues as a patent (or is published as a patent application publication) and the patent document is placed on the USPTO web page, when the patent document is retrieved and viewed via a web browser, the URL is interpreted as a valid HTML code and it becomes a live web link. When a user clicks on the link with a mouse, the user will be transferred to another web page identified by the URL, if it exists, which could be a commercial web site. USPTO policy does not permit the USPTO to link to any commercial sites since the USPTO exercises no control over the organization, views or accuracy of the information contained on these outside sites. If hyperlinks and/or other forms of browser-executable code are embedded in the text of the patent application, examiners should object to the specification and indicate to applicants that the embedded hyperlinks and/or other forms of browser-executable code are impermissible and require deletion."

Correction is required.

4) The instant specification does not comply with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. Table 1 of page 9 of the instant specification discusses a specific amino acid sequence without employing a sequence identifier. Correction is required. See M.P.E.P. 2422.03.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5) Claims 1 to 7 and 12 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed specific and substantial credible utility. These claims are drawn to an isolated nucleic acid molecule encoding a polypeptide comprising the amino acid sequence presented in SEQ ID NO:2 of the instant application. The instant application has provided a description of isolated DNA encoding a putative human receptor protein comprising SEQ ID NO:2, and the protein encoded thereby. The instant application discloses that the protein identified therein as "57242" (SEQ ID NO:2) is a "novel human G protein-coupled receptor" that is expressed in adipose tissue, where it is up regulated during adipocyte differentiation, and down regulated under conditions that affect adipocyte metabolism and in a mouse obesity model. The instant specification does not disclose whether changes in the expression levels of "57242" is a causal factor in alterations in adipocyte activity or a consequence thereof. Further, the instant specification does not identify a single compound which specifically activates or inhibits "57242" activity nor does it identify a specific

physiological response which has been shown to be mediated by that receptor in response to a particular agonist or antagonist.

Whereas the evidence of record supports a conclusion that "57242" **may** play a role in lipid metabolism, that evidence does not support a conclusion that "57242" plays **a particular role** in that process. It is well known in the art that the ligand-activation of G protein-coupled receptors can have a plurality of different stimulatory and/or inhibitory effects, depending upon the particular receptor being activated and the cell in which it is expressed. Whereas a recombinant cell expressing "57242" could be employed to identify agonist and antagonist thereto, this information is of no practical utility in currently available form because the information provided in the instant specification does not allow one to predict whether the administration of a "57242" agonist to an individual will stimulate or inhibit lipid metabolism, stimulate or inhibit adipocyte proliferation, or produce some other, as yet, unforeseen effect. Without knowing what role, if any, that "57242" plays in lipid metabolism an artisan could not employ binding information obtained from therefrom in a specific and practical application.

In the decision of *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966) the court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", " [u]nless and

> until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", " [i]t is not a reward for the search, but compensation for its successful conclusion."

To employ a "57242" protein of the instant invention, or a recombinant cell expressing that protein, to identify agonist and antagonists thereto does not constitute a specific and substantial utility because such a process does not provide a specific benefit in currently available form. The information derived from such a process can not be put to practical use until the additional experimentation needed to determine if a compound identified thereby is stimulatory or inhibitory and to identify those physiological activities which are modulated by that compound has been completed.

Further, neither the instant specification nor the art of record identifies even a single disease or disorder which **has been shown** to be associated with a "57242" protein of the instant invention. Since a "57242" protein of the instant invention has not been shown to be differentially expressed in any disease or disorder beyond the OB mouse model, the protein encoded by the claimed nucleic acid does not have immediate utility in a diagnostic capacity. One would not diagnose obesity by measuring the expression level of "57242" in an individual simply because obesity is defined by body weight. If one found elevated levels of "57242" in the adipose tissue of an individual having a "normal" body weight then one would certainly not conclude that the individual under examination was obese. Conversely, if one detected "normal" levels of "57242" in a visibly obese individual one would not conclude that the individual in question was not obese. This is also true for anorexia and cachexia, which one would not diagnose by measuring the levels of "57242" in adipose tissue.

It is clear from the instant specification that "57242" protein is what is termed an "orphan receptor" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, "57242" protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant claims are drawn to an isolated nucleic acid encoding a protein of as yet undetermined function or biological significance. There is absolutely no evidence of record or any line of reasoning that would support a conclusion the a protein of the instant invention is associated in any way with the plurality of causally unrelated disorders that are listed in paragraphs 59, 61, 66 and 69 of the instant specification. Until some actual and specific significance can be attributed to that protein which identified in the specification as "57242", or the gene encoding then, the instant invention is incomplete. The protein of the instant invention is a compound which is structurally analogous to proteins which are known in the art as G protein-coupled receptors. In the absence of a knowledge of the natural ligands or biological significance of this particular protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances that inhibit its activity is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a credible, substantial and specific "real world" use for the "57242" protein described there then the claimed

invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

The text on pages 54 to 57 of the instant specification discloses that the claimed nucleic acid and the "57242" protein it encodes may serve as markers for chromosomal mapping, tissue typing and in forensic biology. The employment of a protein of the instant invention, or a nucleic acid encoding that protein, as a chromosomal or tissue specific marker is not a substantial or specific utility. All cDNAs can be employed as chromosomal markers. Further, all human proteins can invariably be classified into two categories, those which are expressed in a tissue or developmentally specific manner and those which are expressed ubiquitously. It can be alleged that any protein which is expressed in a tissue specific manner can be employed to detect the tissue in which it is expressed in a sample. Alternately, a human protein which is expressed ubiquitously can be employed to detect the presence of any human tissue in a sample. Such utilities are analogous to the assertion that a particular protein can be employed as a molecular weight marker, which is neither a specific or substantial utility.

One could just as readily argue that any purified compound having a known structure could be employed as an analytical standard in such processes as nuclear magnetic resonance (NMR), infrared spectroscopy (IR), and mass spectroscopy as well as in polyacrylamide gel electrophoresis (PAGE), high performance liquid chromatography (HPLC) and gas chromatography. None of these processes could be practiced without either calibration standards having known molecular structures or, at least, a range of molecular weight markers having known molecular weights. One could further extrapolate upon this premise by asserting that any item having a fixed measurable parameter can be employed to calibrate any machine or process which measures that parameter. For example, any item having a constant mass within an acceptable range can be employed to calibrate a produce scale in a grocery store. The calibration of produce scales is certainly an important function since most states require produce scales to be calibrated and certified. Therefore, to accept Applicant's arguments that any nucleic acid encoding any protein of human origin is useful as a marker would be comparable to conceding that any object of fixed mass has *prima facie* utility as a weight standard, irrespective of any other properties possessed by that object. It was just such applications that the court appeared to be referring to when it expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation (*Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966)). Because the steroid compound which was the subject of that decision had a known structure and molecular weight it could have readily been employed as a molecular standard at that time. Further, because that compound was a

hydrocarbon it certainly could have been employed in the well known process of combustion for purposes of lighting and/ or the generation of heat. The generation of heat by combustion of hydrocarbons certainly was and remains an important process. Irrespective of such obvious utilities, the court still held that the compound produced by the process at issue in *Brenner v. Manson* did not have a specific and substantial utility.

To grant Applicant a patent encompassing an isolated nucleic acid encoding a naturally occurring human protein of as yet undetermined biological significance would be to grant Applicant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole areas of scientific development, without compensating benefit to the public" *(Brenner v. Manson, Ibid)*. To grant Applicant a patent on the claimed nucleic acid based upon an assertion that it can be employed as a chromosomal marker or that the "57242" protein encoded thereby can be employed as a tissue marker is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted and would be no different than granting a patent on the process disputed in *Brenner v. Manson* on the premise that the steroid produced thereby was useful as an analytical standard or as a combustible fuel source.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6) Claims 1 to 7 and 12 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

7) Claims 1, 3 to 7 and 12 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant specification does not contain an adequate written description of "a naturally occurring allelic variant" of a polypeptide consisting of the amino acid sequence of SEQ ID NO:2. In the decision of *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for

obtaining the claimed chemical invention. Fiers v. Revel , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Claim 1 encompasses a genus of nucleic acids that are functionally defined by a genus of proteins encoded thereby and a hybridization activity. One of ordinary skill would not reasonably believe that the majority of nucleic acids which meet the hybridization limitations of claim 1 are going to encode a protein, much less "a naturally occurring allelic variant" of a polypeptide consisting of the amino acid sequence of SEQ ID NO:2. Because the instant specification does not identify that structural feature or combination of features which distinguish a naturally occurring variant of the encoded protein from one which has been intentionally modified, the specification fails to provide a precise description of the claimed genus of proteins encompassed by the limitation "a naturally occurring allelic variant of SEQ ID NO:2" "by structure, formula, chemical name, or physical properties" as required by the first paragraph of 35 U.S.C. § 112. Because the instant specification fails to describe the genus of proteins encoded by the claimed nucleic acid it fails to adequately describe the genus of nucleic acid molecules encompassed by the instant claims.

8) Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention. This claim is drawn to a method of producing a specific polypeptide by culturing a host cell of claim 5. Claim 5 is drawn to a host cell

comprising the nucleic acid molecule of claim 1. Claim 1 is not limited to a nucleic acid encoding a protein. The instant specification does not provide the guidance needed to produce a polypeptide by culturing a host cell which does not comprise a nucleic acid molecule encoding that polypeptide.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9) Claims 1 to 7 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The limitation "hybridizes" "under stringent conditions" is conditional and a specific set of definitive conditions are not disclosed in the specification or recited in the claims. Those "stringent" conditions described on page 20 of the instant specification are expressly identified therein as exemplary and, therefore, not limiting.

35 U.S.C. 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under

> the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

10) Claims 1 to 7 and 12 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by the Elshourbagy et al. patent publication (US 2002/0052022 A1). The amino acid sequence presented in SEQ ID NO:2 of the Elshourbagy et al. patent publication is identical to SEQ ID NO:2 of the instant application. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. Because the instant application does not meet the requirements of 35 U.S.C. § 112, first paragraph, for those reasons given above and prior applications Serial Numbered 60/228,409 and 09/942,374 also do not meet those requirements, the prior applications are unavailable under 35 U.S.C. § 120.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN ULM
PRIMARY EXAMINER
GROUP 1800